CLAIMS

1. A polypeptide comprising

(i) a leader sequence, the leader sequence comprising

(a) a secretion pre sequence, and

(b) the following motif:

$$-X_1-X_2-X_3-X_4-X_5-$$

where X_1 is phenylalanine, tryptophan, or tyrosine, X_2 is isoleucine, leucine, valine, alanine or methionine, X_3 is leucine, valine, alanine or methionine, X_4 is serine or threonine and X_5 is isoleucine, valine, alanine or methionine; and

(ii) a desired protein heterologous to the leader sequence.

2. A polypeptide according to Claim 1 wherein X_1 is phenylalanine.

3. A polypeptide according to Claim 1 or 2 wherein X_2 is isoleucine.

4. A polypeptide according to any one of the preceding claims wherein X_3 is valine.

5. A polypeptide according to any one of the preceding claims wherein the amino acids of the motif are included in the polypeptide as substitutes, for naturally occurring amino acids.

6. A polypeptide according to any one of the preceding claims wherein X_5 is isoleucine.

7. A polypeptide according to any one of the preceding claims wherein the motif is -Phe-Ile-Val-Ser-Ile-.

8. A polypeptide according to any one of the preceding claims wherein the secretion pre sequence is an albumin secretion pre sequence or a variant thereof.

9. A polypeptide according to Claim 8 wherein X_1, X_2, X_3, X_4 and X_5 are at positions -20, -19, -18, -17 and -16, respectively, in place of the naturally occurring amino acids at those positions, wherein the numbering is such that the -1 residue is the C-terminal amino acid of the native albumin secretion pro sequence and where X_1, X_2, X_3, X_4 and X_5 are amino acids as defined in any one of Claims 1 to 7.

10. A polypeptide according to Claim 8 or 9 wherein the albumin secretion pre sequence or variant thereof is a human albumin secretion pre sequence or a variant thereof.

11. A polypeptide according to Claim 10 comprising the secretion pre sequence MKWVFIVSILFLFSSAYS.

12. A polypeptide according to any one of the preceding claims wherein the leader sequence comprises a secretion pro sequence.

13. A polypeptide according to Claim 12 wherein the albumin secretion pre sequence or variant thereof is fused by a peptide bond at its C-terminal end to the N-terminal amino acid of a secretion pro sequence, or variant thereof, thereby to form a pre-pro sequence.

14. A polypeptide according to Claim 12 or 13 wherein the secretion pro sequence is an albumin secretion pro sequence or variant thereof.

15. A polypeptide according to Claim 14 wherein the albumin secretion pro sequence is human serum albumin secretion pro sequence or variant thereof.

16. A polypeptide according to Claim 14 or 15 wherein the secretion pro sequence motif is the yeast MFα-1 secretion pro sequence or variant thereof.

17. A polypeptide according to Claim 12 comprising the sequence:

$$MKWVFIVSILFLFSSAYSRY^1Y^2Y^3Y^4Y^5$$

wherein Y^1 is Gly or Ser, Y^2 is Val or Leu, Y^3 is Phe or Asp, Y^4 is Arg or Lys and Y^5 is Arg or Lys, or variants thereof.

18. A polypeptide according to Claim 17 wherein Y^1 is Gly, Y^2 is Val and Y^3 is Phe; or Y^1 is Ser, Y^2 is Leu and Y^3 is Asp.

19. A polypeptide according to Claim 17 or 18 wherein Y^4 is Arg and Y^5 is Arg; Y^4 is Lys and Y^5 is Arg; Y^4 is Lys and Y is Lys; or Y^4 is Arg and Y^5 is Lys.

20. A polypeptide according to any one of claims 1 to 7 wherein at least part of said motif is present in the secretion pre-sequence.

21. A polypeptide according to any one of the preceding claims wherein the sequence of the desired protein is fused at its N-terminal end to the C-terminal amino acid of the leader sequence.

22. A polypeptide according to any one of the preceding claims where the desired protein is albumin or a variant, fragment or fusion thereof.

23 A polypeptide according to Claim 22 wherein the albumin is human albumin.

24. A polypeptide according to any one of Claims 1 to 21 wherein the mature polypeptide is transferrin or a variant, fragment or fusion thereof.

25. A polypeptide according to Claim 24 wherein the transferrin is human transferrin.

26. An isolated polynucleotide comprising a sequence that encodes the motif defined by any preceding claim.

27. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 15.

28. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 16.

29. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 17.

30. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 18.

31. A polynucleotide according to Claim 26 comprising the sequence of SEQ ID No. 34.

32. A polynucleotide according to Claim 30 or 31 comprising the sequence of SEQ ID No. 24.

33. A polynucleotide according to Claim 32 comprising the sequence of SEQ ID No. 25 or a variant thereof, which variant has the leader sequence of SEQ ID No.24 and encodes a variant or fragment of the albumin encoded by SEQ ID No.25.

34. A polynucleotide according to Claim 30 or 31 comprising the sequence of SEQ ID No. 27.

35. A polynucleotide according to Claim 34 comprising the sequence of SEQ ID No. 21 or a variant thereof, which variant has the leader sequence of SEQ ID No.27 and encodes a variant or fragment of the albumin encoded by SEQ ID No.21.

36. A polynucleotide comprising the sequence of SEQ ID No. 21 or fragment thereof.

37. A polynucleotide according to any one of Claims 33, 35 or 36 wherein the polynucleotide comprises a DNA sequence being a contiguous or non-contiguous fusion of a DNA sequence encoding a heterologous protein with either the DNA sequence SEQ ID No. 25 or the DNA sequence SEQ ID No. 21.

38. A polynucleotide which is the complementary strand of a polynucleotide according to any one of claims 26 to 37.

39. A polynucleotide according to any one of Claims 26 to 38 comprising an operably linked transcription regulatory region.

40. A polynucleotide according to Claim 39 wherein the transcription regulatory region comprises a transcription promoter.

41. A self-replicable polynucleotide sequence comprising a polynucleotide according any one of Claims 26 to 40.

42. A cell comprising a polynucleotide according to any one of Claims 26 to 41.

43. A cell according to Claim 42 which is a eukaryotic cell.

44. A cell according to Claim 43 which is a fungal cell.

45. A cell according to Claim 44 which is an *Aspergillus* cell

46. A cell according to Claim 44 which is a yeast cell.

47. A cell according to Claim 46 which is a *Saccharomyces*, *Kluyveromyces, Schizosaccharomyces* or *Pichia* cell.

48. A cell culture comprising a cell according to any one of Claims 42 to 47 and culture medium.

49. A cell culture according to Claim 48 wherein the medium contains a mature desired protein as a result of the production of a polypeptide as defined in any one of Claims 1 to 22.

50. A process for producing a mature desired protein, comprising (1) culturing a cell according to any one of Claims 42 to 47 in a culture medium wherein the cell, as a result of the production of a polypeptide as defined in any one of Claims 1 to 25, secretes a mature desired protein into the culture medium, and (2) separating the culture medium, containing the secreted mature protein, from the cell.

51. A process according to Claim 50 additionally comprising the step of separating the mature desired protein from the medium and optionally further purifying the mature desired protein.

52. A process according to Claim 51 additionally comprising the step of formulating the thus separated and/or purified mature desired protein with a therapeutically acceptable carrier or diluent thereby to produce a therapeutic product suitable for administration to a human or an animal.